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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,942	03/05/2002	Robert L. Campbell	41552	8014

26253 7590 04/28/2005

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EXAMINER	
BRUSCA, JOHN S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,942	CAMPBELL ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-128* is/are pending in the application.

4a) Of the above claim(s) *16,17 and 31-127* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-15 and 18-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to comply*.

DETAILED ACTION

1. This application has been reassigned to a new examiner.

Sequence Rule Compliance

2. The computer readable form of the sequence listing filed 09 March 2005 has been entered. The corresponding paper copy of the sequence listing filed 09 March 2005 was not accompanied by a formal request to amend the specification by its entry. In response to this Office action please resubmit a paper copy of the sequence listing with a statement directing entry of the paper copy of the sequence listing into the specification as noted in the attached Notice to Comply.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a non-provisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

4. The Office has recognized the applicant's request for priority to prior U.S. Application No. 09/359260 as indicated in the filing receipt of the instant application. However the application file does not show an amendment to the first sentence to claim such priority. The applicants are requested to amend the specification to perfect the claim for domestic priority to the parent application.

Power of Attorney and Correspondence Address

5. The following is a summary of the requests by the applicants to enter a power of attorney and change the correspondence address:

1) The Rule 63 Declaration filed at the application filing date lists David Highet as having power of attorney.

2) An associate power of attorney statement was filed on 20 May 2004 that was signed by Jaconda Wagner who is not of record. The statement was therefore not recognized by the Office. A letter sent by the Office stating the statement was not recognized due to abolition of the associate power of attorney practice was incorrect because the statement was filed prior to ending associate power of attorney practice.

3) A change of correspondence address request was filed on 20 May 2004 that was signed by Maria Aaebius, who is not of record. The request is not recognized by the Office.

4) A change of correspondence address request was filed on 26 July 2004 was filed that was signed by Garrett Davis, who is not of record. The request is not recognized by the Office.

5) A change of correspondence address request was filed on 12 November 2004 that was signed by Leonid Thenor, who is not of record. The request is not recognized by the Office.

6) A change of correspondence address request was filed on 16 March 2005 that was signed by David Highet, who is of record. The request is accepted by the Office and the

current correspondence address is David W. Highet, VP and Chief IP Counsel, Becton, Dickinson and Company, 1 Becton Drive, MC 110, Franklin Lakes, NJ 07417-1880.

Claim Rejections - 35 USC § 101

6. The rejection of claims 1-15 and 18-30 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter in the Office action mailed 11 August 2004 is withdrawn in view if the arguments presented by the applicants in pages 24-28 of their response filed 12 November 2004.

Claim Objections

7. The objection to the claims in the Office action mailed 11 August 2004 is withdrawn in view of the amendment to the claims filed 09 March 2005.

Claim Rejections - 35 USC § 112

8. The rejection of claims 1-15 and 18-30 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 11 August 2004 is withdrawn in view of the amendment to the claims filed 09 March 2005.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must assay for the effect of a peptide library on alteration of production of antibiotics, steroids, carbohydrates, lipids, and nucleic acids in cultured cells. For the reasons discussed below there would be an unpredictable amount of experimentation required to use the claimed method.

b) The specification does not present specific guidance for practicing the claimed method.

c) The specification does not present working examples of the claimed method.

d) The nature of the invention, screening of the effect of peptide libraries, is complex.

e) A search of the prior art did not reveal use of peptides to alter production of antibiotics, steroids, carbohydrates, lipids, and nucleic acids in cultured cells.

f) The skill of those in the art of cell culture assays is high.

g) The prior art does not predict whether the claimed method can be used.

h) The claims are broad in that they are drawn to a method without experimental support that shows that it can be used.

The skilled practitioner would first turn to the instant specification for guidance in practicing the claimed method, however the specification does not provide such guidance. The skilled practitioner would next turn to the prior art for such guidance, however the prior art does not show such guidance. Finally, said practitioner would turn to trial and error experimentation to practice the claimed method. Such represents undue experimentation.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Independent claim 128 and dependent claims 3-10, 13-15, and 18-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Lam et al. (U.S. Patent No. 5,510,240 as further evidenced by Invitrogen catalog.

The claims are drawn to a method of screening compounds by assaying the effect of members of the library in culture medium by measuring an effect of the compound on the properties of the medium. The property of the medium is correlated with a property of the compound. A subset of the library is rescreened that meets a predetermined range of properties as assessed in the first screen. In some embodiments the property of the medium is a function of the property and the compound assayed. In some embodiments the second screen includes compounds not present in the first screen and additional properties are measured. In some embodiments the property of the compound is sequence-specific, a whole molecule parameter, or a molecular weight. In some embodiments the compounds are peptides with at least one residue

of limited variability. In some embodiments the medium is seeded with mammalian cell cultures and a property of the medium is growth of the cell culture or altered peptide or protein production. In some embodiments the culture medium is a synthetic medium.

Lam et al. shows in columns 21 and beyond assays of random peptide libraries on beads added to cells in growth media. The peptides are released from the beads to the media and the cultures are assayed for modulation of growth or other parameters. Lam et al. shows a second round of screening can include a subset of the first library in column 17 lines 18-24 and column 22, lines 20-31. Lam et al. shows assay of cytokine release (a polypeptide) from assayed cultures in column 22 line 60 to column 23 line 3, and measurement of toxicity in column 23 lines 3-14, and screening for peptide inhibitors of tumor cell growth in column 45-46. The sequence (and therefore the molecular weight and structure of the entire peptide) is assayed in columns 27-28. Multiple properties of the peptide library are detected in the examples in columns 41-46. Insertion of non-varies residues in the random peptide sequence is shown in column 8, lines 30-32 and column 40. The results of the assays show that the property of the medium is a function of the particular peptide in the medium. Lam et al. shows use of RPMI medium in column 45, but does not show that RPMI medium is a synthetic medium.

Invitrogen catalog shows the content of RPMI medium. Invitrogen catalog shows that RPMI medium consists entirely of defined compounds.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 128 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bause.

Claim 2 is drawn to the method of claim 128 in which peptides are analyzed by space-filling techniques.

Lam et al. shows in columns 21 and beyond assays of random peptide libraries on beads added to cells in growth media. The peptides are released from the beads to the media and the cultures are assayed for modulation of growth or other parameters.

Lam et al does not show characterization of selected peptides by space filling techniques.

Bause shows analysis of peptide sequences that are sites of glycosylation can be aided by consideration of space-filling parameters in figures 2-4 and pages 333-335.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ space-filling techniques to analyze the selected peptides of Lam et al. because Bause shows that such analysis is useful to determine properties of peptides.

17. Claims 128, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al. in view of Vyas et al.

Claims 11 and 12 are drawn to use of isomers of compounds and space-filling analysis in the method of claim 128.

Lam et al. shows in columns 21 and beyond assays of random peptide libraries on beads added to cells in growth media. The peptides are released from the beads to the media and the cultures are assayed for modulation of growth or other parameters.

Lam et al. does not show isomers of peptides or space-filling analysis.

Vyas et al. shows that the structure at the amino terminus of a particular peptide is important for receptor binding in the abstract and throughout. Optical isomers of peptides are

studied on page 3608 to analyze the binding activity of the peptide. Space filling parameters of peptides are shown in figure 5 to further study structural requirements of binding activity.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ space-filling techniques and peptide isomers to analyze the selected peptides of Lam et al. because Vyas et al. show that such analytical techniques are useful to study relationships between peptide structure and activity.

18. Claims 128, 19, 23, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al. in view of Davis et al.

Lam et al. shows in columns 21 and beyond assays of random peptide libraries on beads added to cells in growth media. The peptides are released from the beads to the media and the cultures are assayed for modulation of growth or other parameters.

Lam et al. does not show analysis of a peptide that is a toxin.

Davis et al. shows on pages 685-686 that Corynebacterium diphtheriae toxin is a polypeptide. Davis et al. show throughout that toxin causes a serious disease in humans by blocking protein synthesis.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Lam et al. to determine the properties of medium containing Corynebacterium diphtheriae toxin polypeptides for the purpose of studying the pathogenic effect of the toxin on cell protein synthesis.

Conclusion

19. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the

USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

John S. Brusca 22 April 2005
John S. Brusca
Primary Examiner
Art Unit 1631

jsb

Notice to Comply	Application No.	Applicant(s)	
	10/087942	Campbell et al.	
	Examiner	Art Unit	
	J. Brusca	1631	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: Amino acid sequences listed in claims 27-28 should be identified by a sequence identifier.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
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